University of Basel

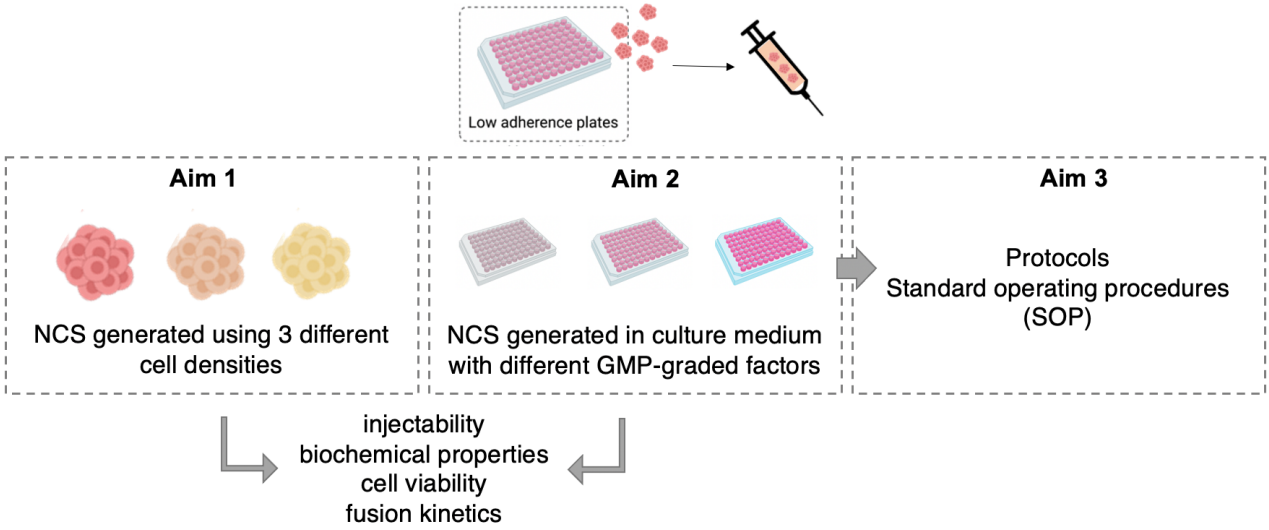
Department of
Biomedical Engineering

MSc thesis proposal

Good manufacturing practice (GMP)-compliant use of human nasal chondrospheres in the treatment of degenerative disc disease

Background. Degenerative disc disease (DDD), a chronic pathology of the intervertebral disc (IVD), is characterized by progressive loss of IVD function, inflammation, and pain. Currently, there is no therapy that is able to stop or reverse degeneration of the IVD. Nasal chondrocytes (NC), cells derived from adult cartilage of the nasal septum, have the superior ability to survive and function in degenerated microenvironments, exhibit features of self-renewal, adapt to heterotopic transplantation sites, and possess robust cartilage-repair capacity *in vivo*. Notably, NC grafts are successfully used at University Hospital Basel to repair cartilage in patients. We have recently demonstrated that NC spheroids (so called nasal chondrospheres, NCS) may have the potential to regenerate the IVD. In order to transfer NCS towards the use in patients, functional/injectable NCS must be fabricated in compliance with regulatory guidelines.

Goal and Aims. The **goal** of this MSc thesis is to develop standard operating procedures (SOP) for NCS use in patients. The candidate will evaluate the injectability, biochemical content, and IVD integration potential of NCS fabricated in increasing cell densities (**Aim 1**) and different GMP-graded factors (**Aim 2**). Best-performing culture condition will serve as basis to write SOP for NCS differentiation for IVD repair (**Aim 3**).



Methods. Human NC (n=5-10) will be isolated from patients and expanded in a medium containing human platelet lysate (hPL). NCS will be generated at three densities (6, 12, 24k NC per NCS) for 7 days in GMP-compliant medium. Once the best density is defined, NCS will be cultured with different GMP-grade culture supplements to resist DDD conditions. NCS (1) morphology, (2) viability, (3) biochemical properties (histology, GAG/Col/DNA), and (4) fusion kinetics in DDD-mimicking conditions will be analyzed before/after pushing NCS through a typical spinal needle. IL-8 in supernatant will be evaluated by ELISA. Protocols leading to the best-performing culture condition will be converted to SOP. Approved GMP SOPs already exist in our laboratory for knee NC grafts.

Significance. GMP-compliant SOPs that describe isolation and expansion of NC and differentiation of NCS will be used in clinical translation of this product to patients with DDD.

Time plan: Duration: 6 months (flexible), Expected start: 2022 (flexible).
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References:
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